Connecting via Winsock to STN

Welcome to STN International! Enter x:X

LOGINID:SSSPTA1644PNH

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS	3	AUG 06	FSTA enhanced with new thesaurus edition
NEWS	4	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS	5	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS	6	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS	7	AUG 27	USPATOLD now available on STN
NEWS	8	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS	9	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS	10	SEP 13	FORIS renamed to SOFIS
NEWS	11	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS	12	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS	13	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS	14	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS	15	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS	16	OCT 19	BEILSTEIN updated with new compounds
NEWS	17	NOV 15	Derwent Indian patent publication number format enhanced
NEWS	18	NOV 19	WPIX enhanced with XML display format
NEWS	19	NOV 30	ICSD reloaded with enhancements
NEWS	20	DEC 04	LINPADOCDB now available on STN
NEWS	21	DEC 14	BEILSTEIN pricing structure to change
NEWS	22	DEC 17	USPATOLD added to additional database clusters
NEWS	23	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS	24	DEC 17	DGENE now includes more than 10 million sequences
NEWS	25	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS	26	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS	27	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS	28	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD
NEWS	29	JAN 02	STN pricing information for 2008 now available

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 09:33:58 ON 14 JAN 2008

=> file medline embase biosis scisearch caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.21 0.21

FILE 'MEDLINE' ENTERED AT 09:34:13 ON 14 JAN 2008

FILE 'EMBASE' ENTERED AT 09:34:13 ON 14 JAN 2008

FILE 'BIOSIS' ENTERED AT 09:34:13 ON 14 JAN 2008

FILE 'SCISEARCH' ENTERED AT 09:34:13 ON 14 JAN 2008

FILE 'CAPLUS' ENTERED AT 09:34:13 ON 14 JAN 2008

=> s VEGF-C peptide
L1 1 VEGF-C PEPTIDE

=> d l1 cbib abs

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
2005:1026967 Document No. 143:332468 Growth factor receptor fragments for use in antitumor therapy. Alitalo, Kari; Jeltsch, Markku M. (Ludwig Institute for Cancer Research, USA; Licentia, Ltd.). PCT Int. Appl. WO 2005087808 A2 20050922, 338 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2005-US7741 20050307. PRIORITY: US 2004-550907P 20040305.

AB The present invention provides materials and methods for antagonizing the function of vascular endothelial growth factor receptors, platelet derived growth factor receptors and other receptors. Soluble binding constructs able to bind vascular endothelial growth factors, platelet derived growth factors, and other ligands are provided. These constructs may be used in treatment of cancers of endothelium and smooth muscle tissues, e.g., carcinomas, squamous cell carcinomas, lymphomas, melanomas, and sarcomas. Thus, chimeric proteins comprising the ligand-binding extracellular

domain, or fragments thereof, of VEGFR-2 and VEGFR-3 fused to the Fc domain of human IgG were prepared with recombinant E. coli. These proteins bound to VEGF-A and/or VEGF-C.

=> s VEGF-D
L2 1689 VEGF-D

=> s l2 and cyclic peptide
L3 2 L2 AND CYCLIC PEPTIDE

=> dup remove l3
PROCESSING COMPLETED FOR L3
L4 2 DUP REMOVE L3 (0 DUPLICATES REMOVED)

=> d l4 1-2 cbib abs

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
2008:13618 Carbohydrate-based VEGF inhibitors. Haag, Tobias; Hughes, Richard A.; Ritter, Gerd; Schmidt, Richard R. (Fachbereich Chemie, Universitaet Konstanz, Konstanz, 78457, Germany). European Journal of Organic Chemistry (36), 6016-6033 (English) 2007. CODEN: EJOCFK. ISSN: 1434-193X. Publisher: Wiley-VCH Verlag GmbH & Co. KGaA.
AB Cyclic peptide-carbohydrates (compds. 1a-c, 2, 33, 34) were designed and synthesized to act as mimetics of loop 2 of the proangiogenic mol. vascular endothelial growth factor D (VEGF-D). The mimetics were designed to inhibit dimerization of the receptors (VEGFR-2 and VEGFR-3) by VEGF-D, and thus have the potential to inhibit angiogenesis. To this end, in the previously described cyclic octapeptide CNEESLIC and the cyclic nonapeptide CGNEESLIC inhibitors derived from VEGF-D loop 2, the NEES tetrapeptide residue was replaced by a carbohydrate scaffold having the amino acid side chain mimics in positions proposed by modeling studies. Attachment of the addnl. amino acids using the Fmoc technol., then formation of the cyclic disulfides, and finally total deprotection afforded the target mols. of which 2 and 34 showed an ability to inhibit the biol. activity of VEGF-D through VEGFR-2 in cell-based assays, albeit at high mimetic concentration

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
2001:545508 Document No. 135:132464 Cyclic peptide inhibitors of VEGF, VEGF-C, and VEGF-D, preparation methods, pharmaceutical compositions, and therapeutic use. Achen, Marc G.; Hughes, Richard A.; Stacker, Steven; Cendron, Angela (Ludwig Institute for Cancer Research, USA). PCT Int. Appl. WO 2001052875 A1 20010726, 102 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US1533 20010118. PRIORITY: US 2000-PV176293 20000118; US 2000-PV204590 20000516.
AB The invention provides monomeric monocyclic peptide inhibitors and dimeric bicyclic peptide inhibitors based on exposed loop fragments of a growth factor protein, e.g. loop 1, loop 2 or loop 3 of VEGF-D , as well as methods of making them, pharmaceutical compns. containing them, and therapeutic methods of use.

```
=> s VEGF-C
L5        4192 VEGF-C

=> s l5 and cyclic peptide
L6           2 L5 AND CYCLIC PEPTIDE

=> dup remove l6
PROCESSING COMPLETED FOR L6
L7           2 DUP REMOVE L6 (0 DUPLICATES REMOVED)

=> d l7 1-2 cbib abs

L7   ANSWER 1 OF 2  SCISEARCH  COPYRIGHT (c) 2008 The Thomson Corporation  on
     STN
2005:903474   The Genuine Article (R) Number: 960XF. Modulating furin activity
     with designed mini-PDX peptides: Synthesis and in vitro kinetic evaluation
     .  Basak A (Reprint); Lotfipour F. Univ Ottawa, Ottawa Hlth Res Inst, Dis
     Aging Program, Reg Prot Chem Ctr, Loeb Bldg, 725 Parkdale Ave, Ottawa, ON
     K1Y 4E9, Canada (Reprint); Univ Ottawa, Ottawa Hlth Res Inst, Dis Aging
     Program, Reg Prot Chem Ctr, Ottawa, ON K1Y 4E9, Canada; Tabriz Univ Med
     Sci, Fac Pharm, Dept Pharmaceut, Tabriz, Iran. abasak@ohri.ca. FEBS
     LETTERS (29 AUG 2005) Vol. 579, No. 21, pp. 4813-4821. ISSN: 0014-5793.
     Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM,
     NETHERLANDS. Language: English.
     *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB        A peptide was designed from reactive site loop structure of alpha 1
     Antitrypsin Portland known as alpha 1 PDX as a novel mini-PDX inhibitor of
     furin.  The sequence was derived from (367-394) that contains the crucial
     furin cleavage motif RIPR382.  A P3 mutant replacing Ile(380) by Len was
     prepared as a first model peptide.  A Cys residue was inserted at each
     terminal of the peptide for purpose of cyclisation which was accomplished
     by air or iodine-induced oxidation.  This mini-PDX peptide both cyclic and
     acyclic form inhibited in vitro furin activity (IC50 in nM) when measured
     against either substrates Boc-RVRR double down arrow MCA or QVEGF-C
     vertical bar Abz-QVHSIIRR double down arrow SLP-Y(NO2)-A-CONH2, Abz =
     2-amino benzoic acid and Y(NO2) = 3-nitro tyrosine vertical bar, latter
     being derived from vascular endothelial growth factor-C (VEGF-
     C) processing site.  The geometrically constrained structure
     mimicking PDX reactive loop is crucial for enzyme inhibition.  Our study
     further revealed that both mini-PDX peptides inactivate furin in a slow
     tight binding manner, with disulfide-bridged cyclic form being slightly
     more potent.  Unlike PDX, these peptides inhibit furin via a different
     mechanistic pathway.  The study provides an alternate strategy for
     development of efficient peptide-based inhibitors of Proprotein
     Convertases including furin.

L7   ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2008 ACS on STN
2001:545508   Document No. 135:132464  Cyclic peptide
     inhibitors of VEGF, VEGF-C, and VEGF-D, preparation
     methods, pharmaceutical compositions, and therapeutic use.  Achen, Marc
     G.; Hughes, Richard A.; Stacker, Steven; Cendron, Angela (Ludwig Institute
     for Cancer Research, USA).  PCT Int. Appl. WO 2001052875 A1 20010726, 102
     pp.  DESIGNATED STATES: W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR,
     BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE,
     GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
     LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,
     SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM,
     AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM,
     CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT,
     SE, SN, TD, TG, TR.  (English).  CODEN: PIXXD2.  APPLICATION: WO
     2001-US1533 20010118.  PRIORITY: US 2000-PV176293 20000118; US
     2000-PV204590 20000516.
```

AB The invention provides monomeric monocyclic peptide inhibitors and dimeric bicyclic peptide inhibitors based on exposed loop fragments of a growth factor protein, e.g. loop 1, loop 2 or loop 3 of VEGF-D, as well as methods of making them, pharmaceutical compns. containing them, and therapeutic methods of use.

```
=> s cyclic peptide
L8       15567 CYCLIC PEPTIDE

=> s l8 and VEGFR-3
L9           1 L8 AND VEGFR-3

=> d l9 cbib abs

L9   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2008 ACS on STN
2008:13618  Carbohydrate-based VEGF inhibitors.  Haag, Tobias; Hughes, Richard
     A.; Ritter, Gerd; Schmidt, Richard R. (Fachbereich Chemie, Universitaet
     Konstanz, Konstanz, 78457, Germany).  European Journal of Organic
     Chemistry (36), 6016-6033 (English) 2007.  CODEN: EJOCFK.  ISSN:
     1434-193X.  Publisher: Wiley-VCH Verlag GmbH & Co. KGaA.
AB   Cyclic peptide-carbohydrates (compds. 1a-c, 2, 33, 34)
     were designed and synthesized to act as mimetics of loop 2 of the
     proangiogenic mol. vascular endothelial growth factor D (VEGF-D).  The
     mimetics were designed to inhibit dimerization of the receptors (VEGFR-2
     and VEGFR-3) by VEGF-D, and thus have the potential to
     inhibit angiogenesis.  To this end, in the previously described cyclic
     octapeptide CNEESLIC and the cyclic nonapeptide CGNEESLIC inhibitors
     derived from VEGF-D loop 2, the NEES tetrapeptide residue was replaced by
     a carbohydrate scaffold having the amino acid side chain mimics in
     positions proposed by modeling studies.  Attachment of the addnl. amino
     acids using the Fmoc technol., then formation of the cyclic disulfides,
     and finally total deprotection afforded the target mols. of which 2 and 34
     showed an ability to inhibit the biol. activity of VEGF-D through VEGFR-2
     in cell-based assays, albeit at high mimetic concentration

=> s GYWLTIWG
L10          0 GYWLTIWG

=> s soluble VEGF-C
L11          7 SOLUBLE VEGF-C

=> s l11 and pd<20010117
   2 FILES SEARCHED...
L12          0 L11 AND PD<20010117

=> s soluble VEGF-D
L13          0 SOLUBLE VEGF-D

=> d his

     (FILE 'HOME' ENTERED AT 09:33:58 ON 14 JAN 2008)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 09:34:13 ON
     14 JAN 2008
L1           1 S VEGF-C PEPTIDE
L2        1689 S VEGF-D
L3           2 S L2 AND CYCLIC PEPTIDE
L4           2 DUP REMOVE L3 (0 DUPLICATES REMOVED)
L5        4192 S VEGF-C
L6           2 S L5 AND CYCLIC PEPTIDE
```

```
L7            2 DUP REMOVE L6 (0 DUPLICATES REMOVED)
L8        15567 S CYCLIC PEPTIDE
L9            1 S L8 AND VEGFR-3
L10           0 S GYWLTIWG
L11           7 S SOLUBLE VEGF-C
L12           0 S L11 AND PD<20010117
L13           0 S SOLUBLE VEGF-D

=> s l2 and soluble
L14         116 L2 AND SOLUBLE

=> s l14 and binds VEGFR-3
L15           0 L14 AND BINDS VEGFR-3

=> s l14 and loop
L16           0 L14 AND LOOP

=> s l14 and pd<20010117
   2 FILES SEARCHED...
L17          10 L14 AND PD<20010117

=> d l17 1-10 cbib abs

L17  ANSWER 1 OF 10     MEDLINE on STN
2001641676.    PubMed ID: 11553610.   Stimulation of beta 1 integrin induces
     tyrosine phosphorylation of vascular endothelial growth factor receptor-3
     and modulates cell migration. Wang J F; Zhang X F; Groopman J E. (Division
     of Experimental Medicine and Hematology/Oncology, Beth Israel Deaconess
     Medical Center, Harvard Medical School, Boston, Massachusetts 02215, USA.
     ) The Journal of biological chemistry, (2001 Nov 9) Vol. 276,
     No. 45, pp. 41950-7.  Electronic Publication: 2001-09-11. Journal code:
     2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.
AB   Interactions between integrins and tyrosine kinase receptors can modulate
     a variety of cell functions.  We observed a cooperative interaction
     between the beta(1) integrin and vascular endothelial growth factor
     receptor-3 (VEGFR-3 or Flt4) that appeared to be required for cell
     migration.  By using VEGFR-3-transfected 293 cells (293/VEGFR-3) or
     primary dermal microvascular endothelial cells (DMEC), we found that
     stimulation with either soluble or immobilized extracellular
     matrix (ECM) proteins, collagen or fibronectin (FN), resulted in the
     increased tyrosine phosphorylation of VEGFR-3 in the absence of a cognate
     ligand.  This increased tyrosine phosphorylation of VEGFR-3 was diminished
     by pretreatment with a blocking antibody against the beta(1) integrin.
     Cross-linking with anti-beta(1) integrin antibody induced a similar degree
     of tyrosine phosphorylation of VEGFR-3.  Stimulation with collagen or FN
     induced an association between beta(1) integrin and VEGFR-3 in both
     293/VEGFR-3 and primary DMEC cells.  Collagen or FN-induced tyrosine
     phosphorylation of VEGFR-3 was inhibited by treatment with cytochalasin D,
     an inhibitor of actin polymerization.  Collagen or FN was able to induce
     the migration of 293/VEGFR-3 or DMEC cells to a limited extent.  However,
     migration was dramatically enhanced when a gradient of the cognate ligand,
     VEGF-D, was added.  VEGF-D failed to
     induce cell migration in the absence of ECM proteins.  Introducing a
     mutation at the kinase domain of VEGFR-3 or treatment with blocking
     antibody against either VEGFR-3 or beta(1) integrin inhibited cell
     migration induced by ECM and VEGF-D, indicating that
     signals from both beta(1) integrin and VEGFR-3 are required for this cell
     function.

L17  ANSWER 2 OF 10     MEDLINE on STN
2001212645.    PubMed ID: 11175851.   Inhibition of lymphangiogenesis with
     resulting lymphedema in transgenic mice expressing soluble VEGF
```

receptor-3. Makinen T; Jussila L; Veikkola T; Karpanen T; Kettunen M I; Pulkkanen K J; Kauppinen R; Jackson D G; Kubo H; Nishikawa S; Yla-Herttuala S; Alitalo K. (Molecular/Cancer Biology Laboratory and Ludwig Institute for Cancer Research, Haartman Institute, University of Helsinki, Helsinki, Finland.) Nature medicine, (2001 Feb) Vol. 7, No. 2, pp. 199-205. Journal code: 9502015. ISSN: 1078-8956. Pub. country: United States. Language: English.

AB The lymphatic vasculature transports extravasated tissue fluid, macromolecules and cells back into the blood circulation. Recent reports have focused on the molecular mechanisms regulating the lymphatic vessels. Vascular endothelial growth factor (VEGF)-C and VEGF-D have been shown to stimulate lymphangiogenesis and their receptor, VEGFR-3, has been linked to human hereditary lymphedema. Here we show that a soluble form of VEGFR-3 is a potent inhibitor of VEGF-C/VEGF-D signaling, and when expressed in the skin of transgenic mice, it inhibits fetal lymphangiogenesis and induces a regression of already formed lymphatic vessels, though the blood vasculature remains normal. Transgenic mice develop a lymphedema-like phenotype characterized by swelling of feet, edema and dermal fibrosis. They survive the neonatal period in spite of a virtually complete lack of lymphatic vessels in several tissues, and later show regeneration of the lymphatic vasculature, indicating that induction of lymphatic regeneration may also be possible in humans.

L17 ANSWER 3 OF 10 MEDLINE on STN

2001190659. PubMed ID: 11129413. Molecular biology of the VEGF and the VEGF receptor family. Clauss M. (MPI fur Physiologische und Klinische Forschung, Bad Nauheim, Germany.. M.Clauss@Kerckhoff.mpg.de) . Seminars in thrombosis and hemostasis, (2000) Vol. 26, No. 5, pp. 561-9. Ref: 106. Journal code: 0431155. ISSN: 0094-6176. Pub. country: United States. Language: English.

AB Vascular endothelial growth factor (VEGF) is the founding member of a still growing family of endothelial cell growth factors. The diverse functions of VEGF and its homologues (PIGF, VEGF-B, VEGF-C, VEGF-D, and VEGF-E) can be explained by their differential binding to the three signaling VEGF receptors. The VEGF family members PIGF and VEGF-B with exclusive binding capacities to the VEGFR-1 can influence monocyte activation and differentiation. The VEGFR-2 and VEGFR-3 binding VEGF homologues, VEGF-C and VEGF-D, are mitogens for both vascular and lymphatic endothelial cells. The orf virus encoded VEGF-E homologue binds and activates only the VEGFR-2 and thus may be the prototype of a vascular endothelial cell-specific growth factor. Further specific activities of VEGF and its homologues result from receptor-specific signaling and differential expression of ligands or receptors. A naturally occurring soluble form of the VEGFR-1 suggests a regulatory role for this receptor. Finally, the production and activation of factors involved in the coagulation/fibrinolytic system provide further evidence for the hypothesis that processes of hemostasis are involved in angiogenesis.

L17 ANSWER 4 OF 10 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

2001064524 EMBASE Inhibition of lymphangiogenesis with resulting lymphedema in transgenic mice expressing soluble VEGF receptor-3. Makinen T.; Jussila L.; Veikkola T.; Karpanen T.; Kettunen M.I.; Pulkkanen K.J.; Kauppinen R.; Jackson D.G.; Kubo H.; Nishikawa S.-I.; Yla-Herttuala S.; Alitalo K.. K. Alitalo, Molecular/Cancer Biology Laboratory, Ludwig Institute Cancer Research, University of Helsinki, Helsinki, Finland. kari.alitalo@helsinki.fi. Nature Medicine Vol. 7, No. 2, pp. 199-205 2001.
Refs: 47.
ISSN: 1078-8956. CODEN: NAMEFI

Pub. Country: United States. Language: English. Summary Language: English.
Entered STN: 20010301. Last Updated on STN: 20010301

AB The lymphatic vasculature transports extravasated tissue fluid, macromolecules and cells back into the blood circulation. Recent reports have focused on the molecular mechanisms regulating the lymphatic vessels. Vascular endothelial growth factor (VEGF)-C and VEGF-D have been shown to stimulate lymphangiogenesis and their receptor, VEGFR-3, has been linked to human hereditary lymphedema. Here we show that a soluble form of VEGFR-3 is a potent inhibitor of VEGF-C/VEGF-D signaling, and when expressed in the skin of transgenic mice, it inhibits fetal lymphangiogenesis and induces a regression of already formed lymphatic vessels, though the blood vasculature remains normal. Transgenic mice develop a lymphedema-like phenotype characterized by swelling of feet, edema and dermal fibrosis. They survive the neonatal period in spite of a virtually complete lack of lymphatic vessels in several tissues, and later show regeneration of the lymphatic vasculature, indicating that induction of lymphatic regeneration may also be possible in humans.

L17 ANSWER 5 OF 10 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

2000439559 EMBASE Molecular biology of the VEGF and the VEGF receptor family.
Clauss M.. Dr. M. Clauss, MPI fur Physiol./Klinische Forsch., Parkstr. 1, 61231 Bad Nauheim, Germany. M.Clauss@Kerckhoff.mpg.de. Seminars in Thrombosis and Hemostasis Vol. 26, No. 5, pp. 561-569 2000.
Refs: 106.
ISSN: 0094-6176. CODEN: STHMBV
Pub. Country: United States. Language: English. Summary Language: English.
Entered STN: 20001229. Last Updated on STN: 20001229

AB Vascular endothelial growth factor (VEGF) is the founding member of a still growing family of endothelial cell growth factors. The diverse functions of VEGF and its homologues (PIGF, VEGF-B, VEGF-C, VEGF-D, and VEGF-E) can be explained by their differential binding to the three signaling VEGF receptors. The VEGF family members PIGF and VEGF-B with exclusive binding capacities to the VEGFR-1 can influence monocyte activation and differentiation. The VEGFR-2 and VEGFR-3 binding VEGF homologues, VEGF-C and VEGF-D, are mitogens for both vascular and lymphatic endothelial cells. The orf virus encoded VEGF-E homologue binds and activates only the VEGFR-2 and thus may be the prototype of a vascular endothelial cell-specific growth factor. Further specific activities of VEGF and its homologues result from receptor, specific signaling and differential expression of ligands or receptors. A naturally occurring soluble form of the VEGFR-1 suggests a regulatory role for this receptor. Finally, the production and activation of factors involved in the coagulation/fibrinolytlc system provide further evidence for the hypothesis that processes of hemostasis are involved in angiogenesis.

L17 ANSWER 6 OF 10 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

2001:312317 Document No.: PREV200100312317. Stimulation of beta-1 integrin induces tyrosine phosphorylation of VEGF receptor-3 and modulates cell migration in endothelial cells. Wang, J.-F. [Reprint author]; Zhang, X.-F. [Reprint author]; Groopman, J. E. [Reprint author]. Divisions of Experimental Medicine and Hematology/Oncology, Beth Israel Deaconess Medical Center, HMS, Boston, MA, USA. Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 530a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971. Language: English.

AB Cooperation and interaction between integrins and tyrosine kinase receptors act to regulate endothelial cell proliferation, differentiation,

survival, and migration. We have observed cooperative interaction between the beta-1 integrin and VEGF receptor-3 (VEGFR-3 or Flt4), and this interaction appears to be required for cell migration. Using VEGFR-3-transfected 293 cells (293/VEGFR-3) or primary dermal microvascular endothelial cells (DMEC), we demonstrated that stimulation with either soluble or immobilized extracellular matrix (ECM) protein, collagen, fibronectin or laminin, resulted in the increased tyrosine phosphorylation of VEGFR-3 in the absence of receptor ligands. This increased tyrosine phosphorylation was diminished by pretreatment with a blocking antibody against beta-1 integrin. Cross-linking with anti-beta-1 integrin antibody induced a similar degree of tyrosine phosphorylation of VEGFR-3 in both (293/VEGFR-3) and DMEC. A constitutive association between beta-1 integrin and VEGFR-3 was observed by co-immunoprecipitation analysis, and this association was enhanced by the stimulation with either ligand for beta integrin or VEGFR-3. We further found that collagen or fibronectin was able to induce migration of 293/VEGFR-3 or DMEC to a limited extent; however, migration was significantly enhanced when a VEGF-D gradient was added. VEGF-D failed to induce cell migration in the absence of matrix proteins. Cell migration induced by matrix proteins and/or VEGF-D was inhibited by blocking antibody against either VEGFR-3 or beta-1 integrin. The tyrosine phosphorylation of VEGFR-3 induced by beta-1 integrin engagement, and the cell migration induced by VEGF-D, were each inhibited by pretreatment with GF109203X, a PKC inhibitor, or cytochalasin D, an inhibitor of actin polymerization. Our results suggest that the stimulation of beta-1 integrin cross-activates VEGFR-3 and that this receptor-receptor interaction is required in the process of endothelial cell migration.

L17 ANSWER 7 OF 10 SCISEARCH COPYRIGHT (c) 2008 The Thomson Corporation on STN

2000:955393 The Genuine Article (R) Number: 382BH. Molecular biology of the VEGF and the VEGF receptor family. Clauss M (Reprint). MPI Physiol & Klin Forsch, Parkstr 1, D-61231 Bad Nauheim, Germany (Reprint); MPI Physiol & Klin Forsch, D-61231 Bad Nauheim, Germany. SEMINARS IN THROMBOSIS AND HEMOSTASIS (2000) Vol. 26, No. 5, pp. 561-569. ISSN: 0094-6176. Publisher: THIEME MEDICAL PUBL INC, 333 SEVENTH AVE, NEW YORK, NY 10001 USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Vascular endothelial growth factor (VEGF) is the founding member of a still growing family of endothelial cell growth factors. The diverse functions of VEGF and its homologues (PIGF, VEGF-B, VEGF-C, VEGF -D, and VEGF-E) can be explained by their differential binding to the three signaling VEGF receptors, The VEGF family members PIGF and VEGF-B with exclusive binding capacities to the VEGFR-1 can influence monocyte activation and differentiation. The VEGFR-2 and VEGFR-3 binding VEGF homologues, VEGF-C and VEGF-D, are mitogens for both vascular and lymphatic endothelial cells. The orf virus encoded VEGF-E homologue binds and activates only the VEGFR-2 and thus may be the prototype of a vascular endothelial cell-specific growth factor, Further specific activities of VEGF and its homologues result from receptor-specific signaling and differential expression of ligands or receptors, A naturally occurring soluble form of the VEGFR-1 suggests a regulatory role for this receptor. Finally, the production and activation of factors involved in the coagulation/fibrinolytic system provide further evidence for the hypothesis that processes of hemostasis are involved in angiogenesis.

L17 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

2001:845468 Document No. 136:80311 Stimulation of β1 integrin induces tyrosine phosphorylation of vascular endothelial growth factor receptor-3 and modulates cell migration. Wang, Jian Feng; Zhang, Xue-Feng; Groopman,

Jerome E. (Division of Experimental Medicine and Hematology/Oncology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, 02215, USA). Journal of Biological Chemistry, 276(45), 41950-41957 (English) 2001. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB Interactions between integrins and tyrosine kinase receptors can modulate a variety of cell functions. We observed a cooperative interaction between the β1 integrin and vascular endothelial growth factor receptor-3 (VEGFR-3 or Flt4) that appeared to be required for cell migration. By using VEGFR-3-transfected 293 cells (293/VEGFR-3) or primary dermal microvascular endothelial cells (DMEC), we found that stimulation with either soluble or immobilized extracellular matrix (ECM) proteins, collagen or fibronectin (FN), resulted in the increased tyrosine phosphorylation of VEGFR-3 in the absence of a cognate ligand. This increased tyrosine phosphorylation of VEGFR-3 was diminished by pretreatment with a blocking antibody against the β1 integrin. Crosslinking with anti-β1 integrin antibody induced a similar degree of tyrosine phosphorylation of VEGFR-3. Stimulation with collagen or FN induced an association between β1 integrin and VEGFR-3 in both 293/VEGFR-3 and primary DMEC cells. Collagen or FN-induced tyrosine phosphorylation of VEGFR-3 was inhibited by treatment with cytochalasin D, an inhibitor of actin polymerization Collagen or FN was able to induce the migration of 293/VEGFR-3 or DMEC cells to a limited extent. However, migration was dramatically enhanced when a gradient of the cognate ligand, VEGF-D, was added. VEGF-D failed to induce cell migration in the absence of ECM proteins. Introducing a mutation at the kinase domain of VEGFR-3 or treatment with blocking antibody against either VEGFR-3 or β1 integrin inhibited cell migration induced by ECM and VEGF-D, indicating that signals from both β1 integrin and VEGFR-3 are required for this cell function.

L17 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

2001:108699 Document No. 134:294065 Inhibition of lymphangiogenesis with resulting lymphedema in transgenic mice expressing soluble VEGF receptor-3. Makinen, Taija; Jussila, Lotta; Veikkola, Tanja; Karpanen, Terhi; Keitunen, Mikko I.; Pulkkanen, Kalevi J.; Kauppinen, Risto; Jackson, David G.; Kubo, Hajime; Nishikawa, Shin-Ichi; Yla-Herttuala, Seppo; Alitalo, Kari (Molecular/Cancer Biology Laboratory and Ludwig Institute for Cancer Research, Haartman Institute, University of Helsinki, Kuopio, Finland). Nature Medicine (New York), 7(2), 199-205 (English) 2001. CODEN: NAMEFI. ISSN: 1078-8956. Publisher: Nature America Inc..

AB The lymphatic vasculature transports extravasated tissue fluid, macromols. and cells back into the blood circulation. Recent reports have focused on the mol. mechanisms regulating the lymphatic vessels. Vascular endothelial growth factor (VEGF)-C and VEGF-D have been shown to stimulate lymphangiogenesis and their receptor, VEGFR-3, has been linked to human hereditary lymphedema. Here the authors show that a soluble form of VEGFR-3 is a potent inhibitor of VEGF-C/VEGF -D signaling, and when expressed in the skin of transgenic mice, it inhibits fetal lymphangiogenesis and induces a regression of already formed lymphatic vessels, though the blood vasculature remains normal. Transgenic mice develop a lymphedema-like phenotype characterized by swelling of feet, edema and dermal fibrosis. They survive the neonatal period in spite of a virtually complete lack of lymphatic vessels in several tissues, and later show regeneration of the lymphatic vasculature, indicating that induction of lymphatic regeneration may also be possible in humans.

L17 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

2000:902508 Document No. 134:141845 Molecular biology of the VEGF and the

VEGF receptor family. Clauss, Matthias (MPI fur Physiologische und Klinische Forschung, Bad Nauheim, 61231, Germany). Seminars in Thrombosis and Hemostasis, 26(5), 561-569 (English) 2000. CODEN: STHMBV. ISSN: 0094-6176. Publisher: Thieme Medical Publishers, Inc..

AB A review with 106 refs. Vascular endothelial growth factor (VEGF) is the founding member of a still growing family of endothelial cell growth factors. The diverse functions of VEGF and its homologs (PIGF, VEGF-B, VEGF-C, VEGF-D, and VEGF-E) can be explained by their differential binding to the three signaling VEGF receptors. The VEGF family members PIGF and VEGF-B with exclusive binding capacities to the VEGFR-1 can influence monocyte activation and differentiation. The VEGFR-2 and VEGFR-3 binding VEGF homologs, VEGF-C and VEGF-D, are mitogens for both vascular and lymphatic endothelial cells. The orf virus encoded VEGF-E homolog binds and activates only the VEGFR-2 and thus may be the prototype of a vascular endothelial cell-specific growth factor. Further specific activities of VEGF and its homologs result from receptor-specific signaling and differential expression of ligands or receptors. A naturally occurring soluble form of the VEGFR-1 suggests a regulatory role for this receptor. Finally, the production and activation of factors involved in the coagulation/fibrinolytic system provide further evidence for the hypothesis that processes of hemostasis are involved in angiogenesis.

```
=> s l14 and derivative
L18          3 L14 AND DERIVATIVE

=> dup remove l18
PROCESSING COMPLETED FOR L18
L19           3 DUP REMOVE L18 (0 DUPLICATES REMOVED)

=> d l19 1-3 cbib abs
```

L19 ANSWER 1 OF 3 MEDLINE on STN

2007183885. PubMed ID: 17221843. Vascular endothelial growth factor and angiopoietin are required for prostate regeneration. Wang Gui-Min; Kovalenko Bruce; Huang Yili; Moscatelli David. (Department of Cell Biology and the Kaplan Cancer Center, New York University School of Medicine, New York, New York 10016, USA.) The Prostate, (2007 Apr 1) Vol. 67, No. 5, pp. 485-99. Journal code: 8101368. ISSN: 0270-4137. Pub. country: United States. Language: English.

AB BACKGROUND: The regulation of the prostate size by androgens may be partly the result of androgen effects on the prostatic vasculature. We examined the effect of changes in androgen levels on the expression of a variety of angiogenic factors in the mouse prostate and determined if vascular endothelial growth factor (VEGF)-A and the angiopoietins are involved in the vascular response to androgens. METHODS: Expression of angiogenic factors in prostate was quantitated using real-time PCR at different times after castration and after administration of testosterone to castrated mice. Angiopoietins were localized in prostate by immunohistochemistry and in situ hybridization. The roles of VEGF and the angiopoietins in regeneration of the prostate were examined in mice inoculated with cells expressing soluble VEGF receptor-2 or soluble Tie-2.
RESULTS: Castration resulted in a decrease in VEGF-A, VEGF-B, VEGF-C, placenta growth factor, FGF-2, and FGF-8 expression after 1 day. In contrast, VEGF-D mRNA levels increased. No changes in angiopoietin-1 (Ang-1), angiopoietin-2 (Ang-2), hepatocyte growth factor, VEGF receptor-1, VEGF receptor-2, or tie-2 mRNA levels were observed. Administration of testosterone to castrated mice had the opposite effect on expression of these angiogenic factors. Ang-2 was expressed predominantly in prostate epithelial cells whereas Ang-1 was expressed in epithelium and smooth muscle. Inoculation of mice with cells expressing

soluble VEGF receptor-2 or Tie-2 blocked the increase in vascular density normally observed after administration of testosterone to castrated mice. The soluble receptors also blocked the increase in prostate weight and proliferation of prostatic epithelial cells. CONCLUSION: VEGF-A and angiopoietins are required for the vascular response to androgens and for the ability of the prostate to regenerate in response to androgens.

L19 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
2005:1242960 Document No. 144:11543 Enhancement of antagonist activity of aptamers by conjugation to high molecular weight materials. Calias, Pericles; Cook, Gary P.; Shima, David T.; Adamis, Anthony P.; Ng, Yin-Shan; Robinson, Gregory S.; Turner, David I.; Ganley, Mary A. (Eyetech Pharmaceuticals, Inc., USA). PCT Int. Appl. WO 2005110489 A2 20051124, 91 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2005-US12469 20050413. PRIORITY: US 2004-561601P 20040413; US 2005-658819P 20050304.
AB The invention provides compns. and methods for making and using sterically enhanced aptamer antagonist conjugates which include a nucleic acid sequence having a specific affinity for a target mol. and a sol ., high mol. weight steric group that augments or facilitates the antagonist activity of the aptamer. inhibition of binding to, or interaction with, the target mol. binding partner by the target mol. when bound to the aptamer conjugate. The present invention also provides methods and formulations for ocular delivery of a biol. active mol. by attaching a charged moiety to the biol. active mol. and delivering the biol. active mol. by iontophoresis. Iontophoresis of a biol. active mol. that is conjugated to a high mol. weight neutral moiety, is enhanced by replacing the high mol. weight neutral moiety with a charged mol. of comparable size. Thus, the effect on VEGFR-1 (Flt-1) antagonist activity of conjugation of chemical modified, anti-VEGF oligoribonucleotide to various high mol. weight materials, i.e., PEG, dextran, and CMC, was studied. Also examined was the effects of mol. weight and hydrodynamic volume of the high mol. weight material on
antagonist activity.

L19 ANSWER 3 OF 3 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
2004135971 EMBASE Development of vascular endothelial growth factor receptor (VEGFR) kinase inhibitors as anti-angiogenic agents in cancer therapy. Underiner T.L.; Ruggeri B.; Gingrich D.E.. T.L. Underiner, Cephalon Inc., 145 Brandywine Parkway, West Chester, PA 19380, United States. tunderin@cephalon.com. Current Medicinal Chemistry Vol. 11, No. 6, pp. 731-745 Mar 2004.
Refs: 115.
ISSN: 0929-8673. CODEN: CMCHE7
Pub. Country: Netherlands. Language: English. Summary Language: English.
Entered STN: 20040412. Last Updated on STN: 20040412
AB Among the known angiogenic growth factors and cytokines implicated in the modulation of normal and pathological angiogenesis, the VEGF family (VEGF-A, VEGF-B, VEGF-C, VEGF-D) and their
corresponding receptor tyrosine kinases [VEGFR-1 (Flt-1), VEGFR-2 (Flk-1, KDR), and VEGFR-3 (Flt-4)] play a paramount and indispensable role in regulating the multiple facets of the angiogenic and lymphangiogenic processes, as well as the induction of vascular permeability and

inflammation. The receptor VEGFR-2/KDR is the principal one through which VEGFs exert their mitogenic, chemotactic, and vascular permeabilizing effects on the host vasculature. Increased expression of VEGFs by tumor cells and VEGFR-2/KDR and VEGFR-1/Flt-1 by the tumor-associated vasculature are a hallmark of a variety of human and rodent tumors in vivo and correlates with tumor growth rate, micro-vessel density/proliferation, tumor metastatic potential, and poorer patient prognosis in a variety of malignancies. Approaches to disrupting the VEGF/VEGFR signaling cascade range from biological agents (soluble receptors, anti-VEGF and anti-VEGFR-2 antibodies, and VEGF transcription inhibitors) to small molecule ATP competitive VEGFR inhibitors. Examples from this latter class that are currently in clinical development include compounds from distinct chemical classes such as: indolin-2-ones, anilinoquinazolines, anilinophthalazines, isothiazoles, indolo- and indenocarbazoles. The structure activity relationships, biochemical and pharmacological profile of optimized representatives from each of these classes constitute the subject matter of this review. .COPYRGT. 2004 Bentham Science Publishers Ltd.

```
=> s VEGF-C derivative
L20          0 VEGF-C DERIVATIVE

=> s VEGF-D derivative
L21          0 VEGF-D DERIVATIVE

=> s (alitalo k?/au or koivunen e?/au or kubo h?/U)
'U' IS NOT A VALID FIELD CODE
'U' IS NOT A VALID FIELD CODE
'U' IS NOT A VALID FIELD CODE
'U' IS NOT A VALID FIELD CODE
'U' IS NOT A VALID FIELD CODE
L22       2923 (ALITALO K?/AU OR KOIVUNEN E?/AU OR KUBO H?/U)

=> s (alitalo k?/au or koivunen e?/au or kubo h?/au)
L23       8841 (ALITALO K?/AU OR KOIVUNEN E?/AU OR KUBO H?/AU)

=> s l23 and VEGFR-3 inhibitor
L24          2 L23 AND VEGFR-3 INHIBITOR

=> dup remove l24
PROCESSING COMPLETED FOR L24
L25           2 DUP REMOVE L24 (0 DUPLICATES REMOVED)

=> d l25 1-2 cbib abs

L25  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2008 ACS on STN
2004:510772   Document No. 141:66280  Modulation of vascular endothelial growth
     factor C (VEGF-C)/vascular endothelial growth factor receptor VEGFR-3
     interactions using VEGFR-3 inhibitor for
     treatment of rheumatoid arthritis.  Alitalo, Kari; Paavonen,
     Karri; Konttinen, Yrjo (Finland).  U.S. Pat. Appl. Publ. US 2004120950 A1
     20040624, 32 pp.  (English).  CODEN: USXXCO.  APPLICATION: US 2002-326048
     20021220.
AB   The present invention provides methods for treating human chronic
     arthridites such as rheumatoid arthritis by modulation vascular
     endothelial growth factor C (VEGF-C)/vascular endothelial growth factor
     receptor VEGFR-3 interactions.  VEGFR-3
     inhibitors such as anti-VEGFR-3 antibody, short-interfering RNA
     (siRNA), or VEGFR-3 extracellular domain-containing polypeptides are
     administered at synovial sites.
```

L25 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
2002:555522 Document No. 137:119669 VEGFR-3
inhibitor materials and methods. Alitalo, Kari;
Koivunen, Erkki; Kubo, Hajime (Ludwig Institute for
Cancer Research, USA; Licentia Ltd.). PCT Int. Appl. WO 2002057299 A2
20020725, 149 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA,
BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE,
ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,
OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY,
DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE,
SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-IB99
20020116. PRIORITY: US 2001-262476P 20010117.
AB The present invention relates to the diagnostics, evaluation, and
therapeutic intervention of disorders mediated by the activity of cell
surface receptor VEGFR-3, which activity often is stimulated by VEGFR-3
ligands VEGF-C and VEGF-D. More particularly, the present invention
identifies novel methods and compns. for the inhibition of VEGF-C/D
binding to VEGFR-3. The compns. of the present invention will be useful
the inhibition of angiogenesis and lymphangiogenesis. Many uses of such
compds., for screening samples, imaging, diagnosis, and therapy, are also
provided. For example, in one emobiment, the invention provides an
isolated peptide comprising the formula: X1X2X3X4X5X6X7X8, wherein X1
through X8 are amino acid residues.

=> s l23 and VEGF-C
L26 645 L23 AND VEGF-C

=> s l26 and peptide
L27 24 L26 AND PEPTIDE

=> dup remove l27
PROCESSING COMPLETED FOR L27
L28 15 DUP REMOVE L27 (9 DUPLICATES REMOVED)

=> s l28 and pd<20010117
2 FILES SEARCHED...
L29 6 L28 AND PD<20010117

=> d l29 1-6 cbib abs

L29 ANSWER 1 OF 6 MEDLINE on STN
2001021068. PubMed ID: 11023993. VEGF-C and VEGF-D
expression in neuroendocrine cells and their receptor, VEGFR-3, in
fenestrated blood vessels in human tissues. Partanen T A; Arola J;
Saaristo A; Jussila L; Ora A; Miettinen M; Stacker S A; Achen M G;
Alitalo K. (Molecular/Cancer Biology Laboratory and Department of
Pathology, Haartman Institute, University of Helsinki, 00014 Helsinki,
Finland.) The FASEB journal : official publication of the Federation of
American Societies for Experimental Biology, (2000 Oct) Vol. 14,
No. 13, pp. 2087-96. Journal code: 8804484. ISSN: 0892-6638. Pub.
country: United States. Language: English.
AB Recently, vascular endothelial growth factor receptor 3 (VEGFR-3) has been
shown to provide a specific marker for lymphatic endothelia in certain
human tissues. In this study, we have investigated the expression of
VEGFR-3 and its ligands VEGF-C and VEGF-D in fetal and
adult tissues. VEGFR-3 was consistently detected in the endothelium of
lymphatic vessels such as the thoracic duct, but fenestrated capillaries
of several organs including the bone marrow, splenic and hepatic
sinusoids, kidney glomeruli and endocrine glands also expressed this

receptor. VEGF-C and VEGF-D, which bind both VEGFR-2 and VEGFR-3 were expressed in vascular smooth muscle cells. In addition, intense cytoplasmic staining for VEGF-C was observed in neuroendocrine cells such as the alpha cells of the islets of Langerhans, prolactin secreting cells of the anterior pituitary, adrenal medullary cells, and dispersed neuroendocrine cells of the gastrointestinal tract. VEGF-D was observed in the innermost zone of the adrenal cortex and in certain dispersed neuroendocrine cells. These results suggest that VEGF-C and VEGF-D have a paracrine function and perhaps a role in peptide release from secretory granules of certain neuroendocrine cells to surrounding capillaries.

L29 ANSWER 2 OF 6 MEDLINE on STN

2000011413. PubMed ID: 10542248. Biosynthesis of vascular endothelial growth factor-D involves proteolytic processing which generates non-covalent homodimers. Stacker S A; Stenvers K; Caesar C; Vitali A; Domagala T; Nice E; Roufail S; Simpson R J; Moritz R; Karpanen T; Alitalo K; Achen M G. (Ludwig Institute for Cancer Research, Royal Melbourne Hospital, Parkville, Victoria 3050, Australia.. steven.stacker@ludwig.edu.au) . The Journal of biological chemistry, (1999 Nov 5) Vol. 274, No. 45, pp. 32127-36. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB Vascular endothelial growth factor-D (VEGF-D) binds and activates the endothelial cell tyrosine kinase receptors VEGF receptor-2 (VEGFR-2) and VEGF receptor-3 (VEGFR-3), is mitogenic for endothelial cells, and shares structural homology and receptor specificity with VEGF-C . The primary translation product of VEGF-D has long N- and C-terminal polypeptide extensions in addition to a central VEGF homology domain (VHD). The VHD of VEGF-D is sufficient to bind and activate VEGFR-2 and VEGFR-3. Here we report that VEGF-D is proteolytically processed to release the VHD. Studies in 293EBNA cells demonstrated that VEGF-D undergoes N- and C-terminal cleavage events to produce numerous secreted polypeptides including a fully processed form of M(r) approximately 21,000 consisting only of the VHD, which is predominantly a non-covalent dimer. Biosensor analysis demonstrated that the VHD has approximately 290- and approximately 40-fold greater affinity for VEGFR-2 and VEGFR-3, respectively, compared with unprocessed VEGF-D. In situ hybridization demonstrated that embryonic lung is a major site of expression of the VEGF-D gene. Processed forms of VEGF-D were detected in embryonic lung indicating that VEGF-D is proteolytically processed in vivo.

L29 ANSWER 3 OF 6 MEDLINE on STN

1999023338. PubMed ID: 9808152. Vascular endothelial growth factor (VEGF)-C synergizes with basic fibroblast growth factor and VEGF in the induction of angiogenesis in vitro and alters endothelial cell extracellular proteolytic activity. Pepper M S; Mandriota S J; Jeltsch M; Kumar V; Alitalo K. (Department of Morphology, University Medical Center, Geneva, Switzerland.. michael.pepper@medecine.unige.ch) . Journal of cellular physiology, (1998 Dec) Vol. 177, No. 3, pp. 439-52. Journal code: 0050222. ISSN: 0021-9541. Pub. country: United States. Language: English.

AB Vascular endothelial growth factor-C (VEGF-C) is a recently characterized member of the VEGF family of angiogenic polypeptides. We demonstrate here that VEGF-C is angiogenic in vitro when added to bovine aortic or lymphatic endothelial (BAE and BLE) cells but has little or no effect on bovine microvascular endothelial (BME) cells. As reported previously for VEGF, VEGF-C and basic fibroblast growth factor (bFGF) induced a synergistic in vitro angiogenic response in all three cells lines. Unexpectedly, VEGF and VEGF-C also synergized in the in vitro angiogenic response when assessed on BAE cells. Characterization of VEGF receptor

(VEGFR) expression revealed that BME, BAE, and BLE cell lines express VEGFR-1 and -2, whereas of the three cell lines assessed, only BAE cells express VEGFR-3. We also demonstrate that VEGF-C increases plasminogen activator (PA) activity in the three bovine endothelial cell lines and that this is accompanied by a concomitant increase in PA inhibitor-1. Addition of alpha2-antiplasmin to BME cells co-treated with bFGF and VEGF-C partially inhibited collagen gel invasion. These results demonstrate, first, that by acting in concert with bFGF or VEGF, VEGF-C has a potent synergistic effect on the induction of angiogenesis in vitro and, second, that like VEGF and bFGF, VEGF-C is capable of altering endothelial cell extracellular proteolytic activity. These observations also highlight the notion of context, i.e., that the activity of an angiogenesis-regulating cytokine depends on the presence and concentration of other cytokines in the pericellular environment of the responding endothelial cell.

L29 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN

2002:594892 Document No. 137:150622 Cloning, tissue expression and therapeutic use of Flt4 (VEGFR-3) polypeptides, their polynucleotides, and antibodies in the diagnosis and treatment of cancer. Alitalo, Kari; Aprelikova, Olga; Pajusola, Katri; Armstrong, Elina; Korhonen, Jaana; Kaipainen, Arja (Ludwig Institute for Cancer Research, USA). PCT Int. Appl. WO 2002060950 A2 20020808, 173 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US1784 20020122. PRIORITY: US 1994-340011 19941114; US 1994-169079 19941114; US 1997-901710 19970728; US 2001-765534 20010119.

AB The present invention provide purified Flt4 receptor tyrosine kinase polypeptides and fragments thereof, polynucleotides encoding such polypeptides, antibodies that specifically bind such polypeptides, and uses thereof in the treatment and diagnosis of disease, specifically cancer.

L29 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN

2001:427336 Document No. 135:41380 Cloning and characterization of a gene for a tyrosine phosphorylation-stimulating ligand, VEGF-C, for the FLT4 receptor tyrosine kinase. Alitalo, Kari ; Joukov, Vladimir (Ludwig Institute for Cancer Research, USA; Helsinki University Licensing, Ltd. Oy). U.S. US 6245530 B1 20010612, 68 pp., Cont.-in-part of U.S. Ser. No. 510,133. (English). CODEN: USXXAM. APPLICATION: US 1996-585895 19960112. PRIORITY: US 1995-510133 19950801.

AB Provided are protein and cDNA sequences of a tyrosine phosphorylation-stimulating ligand, VEGF-C, for the receptor tyrosine kinase, Flt4. VEGF-C, a 23 kDa protein that binds the FLT4 receptor tyrosine kinase and stimulates tyrosine phosphorylation of FLT4 is characterized and a cDNA. The ligand is of potential therapeutic use in controlling the proliferation of endothelial cells. The protein was purified from conditioned medium of PC-3 cell culture by affinity chromatog. A cDNA encoding the ligand was cloned by PCR. The cDNA encoded a protein of approx. 47 kDa that appears to be a precursor that is processed via a 32 kDa intermediate to the mature 23 kDa form that forms a dimer. Alternate splicing of the mRNA appears to occur in response to hypoxia. High-level expression of the gene from the K14 keratin promoter in transgenic mice led to abundant growth of lymphatic vessels in the skin. Also provided are vectors encoding the ligands, pharmaceutical

compns. and diagnostic reagents.

L29 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
1998:151220 Document No. 128:213742 Vascular endothelial cell growth factor D (VEGF-D) and a cDNA encoding and their uses. Achen, Marc G.; Wilks, Andrew F.; Stacker, Steven A.; Alitalo, Kari (Ludwig Institute for Cancer Research, USA; Helsinki University Licensing Ltd., Oy). PCT Int. Appl. WO 9807832 A1 19980226, 101 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US14696 19970821. PRIORITY: AU 1996-1825 19960823; US 1996-23751 19960823; AU 1996-3554 19961111; US 1996-31097 19961114; AU 1997-4954 19970205; US 1997-38814 19970210; AU 1997-7435 19970619; US 1997-51426 19970701.
AB VEGF-D, a new member of the PDGF family of growth factors, which among other things stimulates endothelial cell proliferation and angiogenesis and increases vascular permeability, is described. A cDNA encoding it is cloned. Methods for manufacture of VEGF-D, antibodies and other antagonists to it, transgenic cells for manufacture of the protein, pharmaceutical compns. containing it, and its therapeutic and diagnostic uses are also described. An EST clone encoding a novel member of the VEGF family was identified during a database search. This partial sequence was used to probe a human breast cDNA library and a full-length clone obtained. The protein shows amino acid sequence similarities to VEGF-C and to Tie-2 ligand 1. A bioassay was used to demonstrate that VEGF-D bound the gene KDR receptor and stimulated endothelial cell proliferation.

=> s l23 and VEGF-D
L30 307 L23 AND VEGF-D

=> s l30 and peptide
L31 18 L30 AND PEPTIDE

=> s l31 and pd<20010117
2 FILES SEARCHED...
L32 9 L31 AND PD<20010117

=> d l32 1-9 cbib abs

L32 ANSWER 1 OF 9 MEDLINE on STN
2001021068. PubMed ID: 11023993. VEGF-C and VEGF-D expression in neuroendocrine cells and their receptor, VEGFR-3, in fenestrated blood vessels in human tissues. Partanen T A; Arola J; Saaristo A; Jussila L; Ora A; Miettinen M; Stacker S A; Achen M G; Alitalo K. (Molecular/Cancer Biology Laboratory and Department of Pathology, Haartman Institute, University of Helsinki, 00014 Helsinki, Finland.) The FASEB journal : official publication of the Federation of American Societies for Experimental Biology, (2000 Oct) Vol. 14, No. 13, pp. 2087-96. Journal code: 8804484. ISSN: 0892-6638. Pub. country: United States. Language: English.
AB Recently, vascular endothelial growth factor receptor 3 (VEGFR-3) has been shown to provide a specific marker for lymphatic endothelia in certain human tissues. In this study, we have investigated the expression of VEGFR-3 and its ligands VEGF-C and VEGF-D in fetal and adult tissues. VEGFR-3 was consistently detected in the endothelium of lymphatic vessels such as the thoracic duct, but fenestrated capillaries of several organs including the bone marrow, splenic and hepatic

sinusoids, kidney glomeruli and endocrine glands also expressed this receptor. VEGF-C and VEGF-D, which bind both VEGFR-2 and VEGFR-3 were expressed in vascular smooth muscle cells. In addition, intense cytoplasmic staining for VEGF-C was observed in neuroendocrine cells such as the alpha cells of the islets of Langerhans, prolactin secreting cells of the anterior pituitary, adrenal medullary cells, and dispersed neuroendocrine cells of the gastrointestinal tract. VEGF-D was observed in the innermost zone of the adrenal cortex and in certain dispersed neuroendocrine cells. These results suggest that VEGF-C and VEGF-D have a paracrine function and perhaps a role in peptide release from secretory granules of certain neuroendocrine cells to surrounding capillaries.

L32 ANSWER 2 OF 9 MEDLINE on STN

2000011413. PubMed ID: 10542248. Biosynthesis of vascular endothelial growth factor-D involves proteolytic processing which generates non-covalent homodimers. Stacker S A; Stenvers K; Caesar C; Vitali A; Domagala T; Nice E; Roufail S; Simpson R J; Moritz R; Karpanen T; Alitalo K; Achen M G. (Ludwig Institute for Cancer Research, Royal Melbourne Hospital, Parkville, Victoria 3050, Australia.. steven.stacker@ludwig.edu.au) . The Journal of biological chemistry, (1999 Nov 5) Vol. 274, No. 45, pp. 32127-36. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB Vascular endothelial growth factor-D (VEGF-D) binds and activates the endothelial cell tyrosine kinase receptors VEGF receptor-2 (VEGFR-2) and VEGF receptor-3 (VEGFR-3), is mitogenic for endothelial cells, and shares structural homology and receptor specificity with VEGF-C. The primary translation product of VEGF-D has long N- and C-terminal polypeptide extensions in addition to a central VEGF homology domain (VHD). The VHD of VEGF-D is sufficient to bind and activate VEGFR-2 and VEGFR-3. Here we report that VEGF-D is proteolytically processed to release the VHD. Studies in 293EBNA cells demonstrated that VEGF-D undergoes N- and C-terminal cleavage events to produce numerous secreted polypeptides including a fully processed form of M(r) approximately 21,000 consisting only of the VHD, which is predominantly a non-covalent dimer. Biosensor analysis demonstrated that the VHD has approximately 290- and approximately 40-fold greater affinity for VEGFR-2 and VEGFR-3, respectively, compared with unprocessed VEGF-D. In situ hybridization demonstrated that embryonic lung is a major site of expression of the VEGF-D gene. Processed forms of VEGF-D were detected in embryonic lung indicating that VEGF-D is proteolytically processed in vivo.

L32 ANSWER 3 OF 9 EMBASE

2000353140 EMBASE VEGF-C and VEGF-D expression in neuroendocrine cells and their receptor, VEGFR-3, in fenestrated blood vessels in human tissues. Partanen T.A.; Arola J.; Saaristo A.; Jussila L.; Ora A.; Miettinen M.; Stacker S.A.; Achen M.G.; Alitalo K.. K. Alitalo, Molecular/Cancer Biology Laboratory, Ludwig Institute for Cancer Research, University of Helsinki, Haartmaninkatu 3, 00014 Helsinki, Finland. Kari.Alitalo@Helsinki.fi. FASEB Journal Vol. 14, No. 13, pp. 2087-2096 2000.
Refs: 44.
ISSN: 0892-6638. CODEN: FAJOEC
Pub. Country: United States. Language: English. Summary Language: English.
Entered STN: 20001102. Last Updated on STN: 20001102

AB Recently, vascular endothelial growth factor receptor 3 (VEGFR-3) has been shown to provide a specific marker for lymphatic endothelia in certain human tissues. In this study, we have investigated the expression of VEGFR-3 and its ligands VEGF-C and VEGF-D in fetal and

adult tissues. VEGFR-3 was consistently detected in the endothelium of lymphatic vessels such as the thoracic duct, but fenestrated capillaries of several organs including the bone marrow, splenic and hepatic sinusoids, kidney glomeruli and endocrine glands also expressed this receptor. VEGF-C and VEGF-D, which bind both VEGFR-2 and VEGFR-3 were expressed in vascular smooth muscle cells. In addition, intense cytoplasmic staining for VEGF-C was observed in neuroendocrine cells such as the α cells of the islets of Langerhans, prolactin secreting cells of the anterior pituitary, adrenal medullary cells, and dispersed neuroendocrine cells of the gastrointestinal tract. VEGF-D was observed in the innermost zone of the adrenal cortex and in certain dispersed neuroendocrine cells. These results suggest that VEGF-C and VEGF-D have a paracrine function and perhaps a role in peptide release from secretory granules of certain neuroendocrine cells to surrounding capillaries.

L32 ANSWER 4 OF 9 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
2000:512474 Document No.: PREV200000512474. VEGF-C and VEGF-D expression in neuroendocrine cells and their receptor, VEGFR-3, in fenestrated blood vessels in human tissues. Partanen, Taina A.; Arola, Johanna; Saaristo, Anne; Jussila, Lotta; Ora, Ari; Miettinen, Markku; Stacker, Steven A.; Achen, Marc G.; Alitalo, Kari [Reprint author]. Molecular/Cancer Biology Laboratory, Ludwig Institute for Cancer Research, Haartman Institute, University of Helsinki, Haartmaninkatu 3, 00014, Helsinki, Finland. FASEB Journal, (October, 2000) Vol. 14, No. 13, pp. 2087-2096. print.
CODEN: FAJOEC. ISSN: 0892-6638. Language: English.
AB Recently, vascular endothelial growth factor receptor 3 (VEGFR-3) has been shown to provide a specific marker for lymphatic endothelia in certain human tissues. In this study, we have investigated the expression of VEGFR-3 and its ligands VEGF-C and VEGF-D in fetal and adult tissues. VEGFR-3 was consistently detected in the endothelium of lymphatic vessels such as the thoracic duct, but fenestrated capillaries of several organs including the bone marrow, splenic and hepatic sinusoids, kidney glomeruli and endocrine glands also expressed this receptor. VEGF-C and VEGF-D, which bind both VEGFR-2 and VEGFR-3 were expressed in vascular smooth muscle cells. In addition, intense cytoplasmic staining for VEGF-C was observed in neuroendocrine cells such as the alpha cells of the islets of Langerhans, prolactin secreting cells of the anterior pituitary, adrenal medullary cells, and dispersed neuroendocrine cells of the gastrointestinal tract. VEGF-D was observed in the innermost zone of the adrenal cortex and in certain dispersed neuroendocrine cells. These results suggest that VEGF-C and VEGF-D have a paracrine function and perhaps a role in peptide release from secretory granules of certain neuroendocrine cells to surrounding capillaries.

L32 ANSWER 5 OF 9 SCISEARCH COPYRIGHT (c) 2008 The Thomson Corporation on STN
2000:759962 The Genuine Article (R) Number: 359WE. VEGF-C and VEGF-D expression in neuroendocrine cells and their receptor, VEGFR-3, in fenestrated blood vessels in human tissues. Partanen T A; Arola J; Saaristo A; Jussila L; Ora A; Miettinen M; Stacker S A; Achen M G; Alitalo K (Reprint). Univ Helsinki, Haartman Inst, Mol Canc Biol Lab, Haartmaninkatu 3, FIN-00014 Helsinki, Finland (Reprint); Univ Helsinki, Haartman Inst, Mol Canc Biol Lab, FIN-00014 Helsinki, Finland; Univ Helsinki, Haartman Inst, Dept Pathol, FIN-00014 Helsinki, Finland; Armed Forces Inst Pathol, Dept Soft Tissue Pathol, Washington, DC 20306 USA; Royal Melbourne Hosp, Melbourne Tumour Biol Branch, Ludwig Inst Canc Res, Angiogenesis Lab, Parkville, Vic 3050, Australia. FASEB JOURNAL (OCT 2000) Vol. 14, No. 13, pp. 2087-2096. ISSN: 0892-6638.
Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD

20814-3998 USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Recently, vascular endothelial growth factor receptor 3 (VEGFR-3) has been shown to provide a specific marker for lymphatic endothelia in certain human tissues. In this study, we have investigated the expression of VEGFR-3 and its ligands VEGF-C and VEGF-D in fetal and adult tissues. VEGFR-3 was consistently detected in the endothelium of lymphatic vessels such as the thoracic duct, but fenestrated capillaries of several organs including the bone marrow, splenic and hepatic sinusoids, kidney glomeruli and endocrine glands also expressed this receptor. VEGF-C and VEGF-D, which bind both VEGFR-2 and VEGFR-3 were expressed in vascular smooth muscle cells. In addition, intense cytoplasmic staining for VEGF-C was observed in neuroendocrine cells such as the alpha cells of the islets of Langerhans, prolactin secreting cells of the anterior pituitary, adrenal medullary cells, and dispersed neuroendocrine cells of the gastrointestinal tract. VEGF-D was observed in the innermost zone of the adrenal cortex and in certain dispersed neuroendocrine cells. These results suggest that VEGF-C and VEGF-D have a paracrine function and perhaps a role in peptide release from secretory granules of certain neuroendocrine cells to surrounding capillaries.

L32 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

2002:594892 Document No. 137:150622 Cloning, tissue expression and therapeutic use of Flt4 (VEGFR-3) polypeptides, their polynucleotides, and antibodies in the diagnosis and treatment of cancer. Alitalo, Kari; Aprelikova, Olga; Pajusola, Katri; Armstrong, Elina; Korhonen, Jaana; Kaipainen, Arja (Ludwig Institute for Cancer Research, USA). PCT Int. Appl. WO 2002060950 A2 20020808, 173 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US1784 20020122. PRIORITY: US 1994-340011 19941114; US 1994-169079 19941114; US 1997-901710 19970728; US 2001-765534 20010119.

AB The present invention provide purified Flt4 receptor tyrosine kinase polypeptides and fragments thereof, polynucleotides encoding such polypeptides, antibodies that specifically bind such polypeptides, and uses thereof in the treatment and diagnosis of disease, specifically cancer.

L32 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

2001:119862 Document No. 134:290692 VEGF-C and VEGF-D expression in neuroendocrine cells and their receptor, VEGFR-3, in fenestrated blood vessels in human tissues. Partanen, Taina A.; Arola, Johanna; Saaristo, Anne; Jussila, Lotta; Ora, Ari; Miettinen, Markku; Stacker, Steven A.; Achen, Marc G.; Alitalo, Kari (Molecular / Cancer Biology Laboratory and Department of Pathology, Haartman Institute, University of Helsinki, Helsinki, 00014, Finland). FASEB Journal, 14(13), 2087-2096 (English) 2000. CODEN: FAJOEC. ISSN: 0892-6638. Publisher: Federation of American Societies for Experimental Biology.

AB Recently, vascular endothelial growth factor receptor 3 (VEGFR-3) has been shown to provide a specific marker for lymphatic endothelia in certain human tissues. In this study, we have investigated the expression of VEGFR-3 and its ligands VEGF-C and VEGF-D in fetal and adult tissues. VEGFR-3 was consistently detected in the endothelium of lymphatic vessels such as the thoracic duct, but fenestrated capillaries of several organs including the bone marrow, splenic and hepatic

sinusoids, kidney glomeruli and endocrine glands also expressed this receptor. VEGF-C and VEGF-D, which bind both VEGFR-2 and VEGFR-3 were expressed in vascular smooth muscle cells. In addition, intense cytoplasmic staining for VEGF-C was observed in neuroendocrine cells such as the α cells of the islets of Langerhans, prolactin secreting cells of the anterior pituitary, adrenal medullary cells, and dispersed neuroendocrine cells of the gastrointestinal tract. VEGF-D was observed in the innermost zone of the adrenal cortex and in certain dispersed neuroendocrine cells. These results suggest that VEGF-C and VEGF-D have a paracrine function and perhaps a role in peptide release from secretory granules of certain neuroendocrine cells to surrounding capillaries.

L32 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
1999:468435 Document No. 131:83470 Expression vectors and cell lines expressing vascular endothelial growth factor D, and method of treating melanomas. Achen, Marc G.; Stacker, Steven Alan; Alitalo, Kari (Ludwig Institute for Cancer Research, USA). PCT Int. Appl. WO 9933485 A1 19990708, 79 pp. DESIGNATED STATES: W: AU, CA, CN, JP, KR, NZ; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US27373 19981223. PRIORITY: AU 1997-1131 19971224; US 1998-87392 19980529.
AB This invention relates to expression vectors comprising VEGF-D and its biol. active derivs., cell lines stably expressing VEGF-D and its biol. active derivs., and to a method of making a polypeptide using these expression vectors and host cells. Optionally, VEGF-D produced by the cell line of the invention is linked to an epitope tag such as FLAG, hexahistidine, or I-SPY, to facilitate purification of the polypeptide by affinity chromatog. The mammalian cell line may preferably be the 293-EBNA human embryonal kidney cell line, and several Apex-3 plasmid expression constructs are provided. The invention also relates to a method for treating and alleviating melanomas or tumors expressing VEGF-D and various diseases.

L32 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
1998:151220 Document No. 128:213742 Vascular endothelial cell growth factor D (VEGF-D) and a cDNA encoding and their uses. Achen, Marc G.; Wilks, Andrew F.; Stacker, Steven A.; Alitalo, Kari (Ludwig Institute for Cancer Research, USA; Helsinki University Licensing Ltd., Oy). PCT Int. Appl. WO 9807832 A1 19980226, 101 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US14696 19970821. PRIORITY: AU 1996-1825 19960823; US 1996-23751 19960823; AU 1996-3554 19961111; US 1996-31097 19961114; AU 1997-4954 19970205; US 1997-38814 19970210; AU 1997-7435 19970619; US 1997-51426 19970701.
AB VEGF-D, a new member of the PDGF family of growth factors, which among other things stimulates endothelial cell proliferation and angiogenesis and increases vascular permeability, is described. A cDNA encoding it is cloned. Methods for manufacture of VEGF-D, antibodies and other antagonists to it, transgenic cells for manufacture of the protein, pharmaceutical compns. containing it, and its therapeutic and diagnostic uses are also described. An EST clone encoding a novel member of the VEGF family was identified during a database search. This partial sequence was used to probe a human breast cDNA library and a full-length clone obtained. The protein shows amino

acid sequence similarities to VEGF-C and to Tie-2 ligand 1. A bioassay was used to demonstrate that VEGF-D bound the gene KDR receptor and stimulated endothelial cell proliferation.

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	232.46	232.67

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-14.40	-14.40

STN INTERNATIONAL LOGOFF AT 09:47:28 ON 14 JAN 2008